of the outcome of the answers to the remaining questions.

DR. LIPICKY: That's fine.

CHAIRMAN BORER: Okay.

DR. LIPICKY: We can do that.

CHAIRMAN BORER: Let's move on.

DR. LIPICKY: But you've got to answer the questions.

CHAIRMAN BORER: That's what we're doing right now.

Five point two is adverse skin reactions.

DR. LIPICKY: Okay. Fine. so your answer to mortality was?

CHAIRMAN BORER: It's a labeling issue, and we'd like --

DR. LIPICKY: It's a labeling issue.

CHAIRMAN BORER: -- some more information of the specific nature that Steve and Paul have outlined, and Tom.

Okay. Are there sufficient data to conclude that Extraneal is safe with respect to adverse skin reactions?

Anybody want to tackle that? Alan, do you have an opinion here?

DR. HIRSCH: I'm satisfied.

CHAIRMAN BORER: Okay.

DR. HIRSCH: That there is a relationship, but the safety is present. You've satisfied me that it's safe.

CHAIRMAN BORER: Okay. Anybody disagree with that?

How about peritonitis?

PARTICIPANTS: Safe.

CHAIRMAN BORER: Safe. Okay. Loss of membrane permeability, the issue that Dr. Brem raised earlier. Do you have any concerns about that?

DR. HIRSCH: NO.

CHAIRMAN BORER: Okay. Other adverse reactions that we haven't discussed here in this list? Anybody have any? Steve, no?

DR. LIPICKY: Did you see anything else that we should pay attention to?

DR. NISSEN: We've already talked about the hypertension.

CHAIRMAN BORER: Right. Okay. Now we'll go one by one. First, should Extraneal be approved as a peritoneal dialysis solution?

And we'll start at the left-hand side of the table. Dr. Kopp?

DR. KOPP: Yes.

CHAIRMAN BORER: Should Extraneal be approved as a peritoneal dialysis solution? You're saying yes?

DR. KOPP: Yes.

CHAIRMAN BORER: Okay. And let's go on. Maybe you can complete the answer.

If the answer is yes, which you've said it is, should labeling describe Extraneal as a dialysate similar in safety and efficacy to other dialysis solutions?

DR. KOPP: Yes, with regard to the 1.5 and the 2.5.

CHAIRMAN BORER: Okay. An alternative dialysis solution to be used only under specific circumstances? And if so, is that limitation for the use of Extraneal based on its enhanced efficacy under

specific circumstances, or is it based on increase safety concerns?

DR. LIPICKY: I've got to clarify that, I think.

CHAIRMAN BORER: Yes, okay. You can clarify it.

DR. LIPICKY: The notion is he said it can be approved. So now what is the perspective that it is going to be approved for?

One could say it's a dialysis solution. You can use it, but hardly ever, because I'm worried about its mortality and its blood pressure, its cardiovascular stuff, and then you should only use it as a long dwell and only for a couple of days, you know.

So okay. So that's restricting it because it is -- you have a worry.

The other is that it ought to really be unworrisome in another dialysate solution, but still long dwell because that's what it's designed to do the best, but then how are you going to tell people about that without giving them ultra filtration and stuff as

a claim in the labeling?

Or should it just be another dialysis solution? You can use this sometimes, and that's the nuance that's being looked for here, and obviously there's no clear answer, but just sort of looking for how you would lean on that.

CHAIRMAN BORER: Ray, how do we deal with the fact that the company has specifically requested an indication only for --

DR. LIPICKY: We don't care what they requested.

CHAIRMAN BORER: Okay.

DR. LIPICKY: You know, we give them what they get.

(Laughter.)

CHAIRMAN BORER: Okay. Dr. Kopp, do you want to with that clarification?

DR. KOPP: I'm more confused than I was a few minutes ago. But I think the data does suggest that there's some increase in ultra filtration. We've said that we don't know the clinical implications of that, but I think that should be laid out in the

packaging so that the clinician can see there is a 200 mL difference and suggest that the appropriate use is for long dwell indications, but on a chronic basis.

I think the mortality and morbidity issues are sufficiently of low level enough concern that I think it's reasonable that somebody plan on using this on a regular basis. That's my take on it.

CHAIRMAN BORER: Alan?

DR. HIRSCH: Well, I might just second that. I was going to say just simply it's another dialysis solution and leave it at that, but I suppose like other studies we've looked at applied in a long dwell situation as you have presented to us.

CHAIRMAN BORER: Okay. Paul?

DR. ARMSTRONG: Well, you would understand my yes is conditional on Dr. Lipicky's reassurance on the data, the questions I've raised. But that being the case, then I would be yes, and I would answer the second part as has been answered.

CHAIRMAN BORER: Okay. JoAnn?

DR. LINDENFELD: I would say yes. I might like to say it would be indicated for patients who

need enhanced ultra filtration, and then expand that or make it more general when mortality data is known.

I mean, I'm still a little bit concerned about this mortality difference. I know the numbers are very small, but we only have one set of data, and that would be my answer.

CHAIRMAN BORER: Tom?

DR. FLEMING: I think my perspective is in line with what I've heard with my four colleagues, and I would certainly concur with exactly what Paul said. This is subject to the additional analyses that we have requested, several of the committee members have requested be done that relate to further exploration of the data on blood pressure and the data on mortality and cause of mortality and preferably in my view getting enhanced follow-up on mortality.

And as has been suggested, as well, with a plan for post marketing surveillance, but we might come back and discuss that later.

CHAIRMAN BORER: Okay. Mike.

DR. ARTMAN: Yes. I think it should be approved, and I would also favor, I think, what JoAnn

said, that the indication may be for those patients who need enhanced ultra filtration because of these safety concerns.

CHAIRMAN BORER: Dr. Anderson.

DR. ANDERSON: Oh, yes. My answer is yes. I would strongly encourage that we look at the possibility of collecting additional data in the area of viscosity, systemic absorption, and metabolic products.

The whole blood pressure issue somehow bothers me because if I read the table correctly, it's the last data point on the table, and in my research, I would never stop at that. It's out of whack with the rest of it, and I would want to know what's beyond that.

CHAIRMAN BORER: Steve?

DR. NISSEN: I support approval, and I support approval to be used routinely in dialysis, and I would describe in the label the enhanced efficacy of ultra filtration. However, my support is contingent upon an appropriate post marketing program designed to explore the issues of hypertension and its

relationship to mortality.

Now, what form that takes, I'm not prepared to say at this point, but I do think that it just would be wrong to completely ignore a six millimeter blood pressure difference, given what we know about blood pressure and cardiovascular mortality. To just ignore it and wish it away I think would be a mistake for the agency and for the public.

CHAIRMAN BORER: Dr. Brem?

DR. BREM: I support its use as a long dwell alternative to existing solutions.

CHAIRMAN BORER: Okay, and I vote yes also, and I would echo exactly what Steve said and add the issue -- the other that we want to see the other data that have been mentioned by JoAnn and Tom.

Is that sufficient information, Ray? Are there any other --

DR. LIPICKY: That's fine.

CHAIRMAN BORER: Great. Well, thank you very much. We're all done.

Tomorrow morning we will be meeting again, and I believe it is at 8:30.

(Whereupon, at 5:10 p.m., the Advisory Committee meeting was adjourned, to reconvene at 8:30 a.m., Friday, August 10, 2001.)

CERTIFICATE

This is to certify that the foregoing transcript in the matter of: Meeting of the Cardiovascular and Renal Drugs Advisory Committee

Before: DHHS/PHS/FDA/CDER

Date: August 9, 2001

Place: Bethesda, MD

represents the full and complete proceedings of the aforementioned matter, as reported and reduced to typewriting.